

Notice of Allowability	Application No.	Applicant(s)	
	10/561,775	VERENTCHIKOV ET AL.	
	Examiner Michael Maskell	Art Unit 2881	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. This communication is responsive to communications filed 12/10/2007.

2. The allowed claim(s) is/are 1,3-48 and 50-61.

3. Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some* c) None of the:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. _____.

3. Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. CORRECTED DRA WINGS (as "replacement sheets") must be submitted.

(a) including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
1) hereto or 2) to Paper No./Mail Date _____.

(b) including changes required by the attached Examiner's Amendment / Comment or in the Office action of
Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. DEPOS IT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|---|---|
| 1. <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date _____. |
| 3. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date <u>02/07/07;01/09/2008</u> | 7. <input type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____. |

DETAILED ACTION

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Terry Callaghan on 01/08/2008. The application has been amended as follows:

Canceled claims 2, 49, and 79 (claims 62-78 previously canceled).

Amended claims 1, 10, 33, 48, and 61 as follows:

- claim 1 amended to include claim 2
- claim 10 rewritten in independent form
- claim 33 written to depend from claim 1
- claim 48 amended to include claims 49 and 2
- claim 61 amended to include claim 2

The claims should now read as follows:

1. A multi-reflecting time-of-flight mass spectrometer (MR-TOF MS) comprising:
 - an ion source;
 - an ion receiver downstream from said ion source;
 - at least one ion mirror assembly intermediate said ion source and said ion receiver and elongated in a shift direction for improving sensitivity and resolution of the MR-TOF MS;

a drift space intermediate said ion mirror assembly; and

a lens assembly disposed within said drift space along at least one shift direction and with a period in said shift direction corresponding to ion shift per integer number of ion reflections,

said ion source, ion receiver, ion mirror assembly and said drift space arranged to provide a folded ion path between said ion source and said ion receiver composed of at least one reflection by said ion mirror assembly for separating ions in time according to their mass-to-charge ratio (m/z) so that a flight time of the ions is substantially independent of ion energy.

2. (Canceled)
3. The MR-TOF MS as defined in claim 1, further comprising: a timed ion selector including one of a Bradbury-Nielsen ion gate, a parallel plate deflector, and a control grid within said ion receiver.
4. The MR-TOF MS as defined in claim 1, wherein said ion source comprises one of an ion storage device and an ion accelerator.
5. The MR-TOF MS as defined in claim 1, wherein said ion source comprises a continuous ion source.
6. The MR-TOF MS as defined in claim 1, wherein said ion source comprises one of a SIMS, a MALDI, and an IR-MALDI.
7. The MR-TOF MS as defined in claim 5, wherein said ion source comprises one of an ESI, an APCI, an APPI, an EI, a CI, a PI, an ICP, a gas-filled MALDI, an atmospheric MALDI, a gaseous ion reaction cell, a DC/field asymmetric ion mobility spectrometer, and a fragmentation cell.

8. The MR-TOF MS as defined in claim 1, wherein said ion receiver includes an ion detector having an extended dynamic range.
9. The MR-TOF MS as defined in claim 1, wherein said ion receiver comprises a gas-filled cell selected from one of a fragmentation cell, a molecular reaction cell, an ion reaction cell, electron capture dissociation, ion capture dissociation, a soft deposition cell, and a cell for surface ion dissociation.
10. A multi-reflecting time-of-flight mass spectrometer (MR-TOF MS) comprising:
 - an ion source;
 - an ion receiver downstream from said ion source;
 - at least one ion mirror assembly intermediate said ion source and said ion receiver and elongated in a shift direction for improving sensitivity and resolution of the MR-TOF MS; and
 - a drift space intermediate said ion mirror assembly,
 - said ion source, ion receiver, ion mirror assembly and said drift space arranged to provide a folded ion path between said ion source and said ion receiver composed of at least one reflection by said ion mirror assembly for separating ions in time according to their mass-to-charge ratio (m/z) so that a flight time of the ions is substantially independent of ion energy,
 - wherein said ion mirror assembly comprises a plurality of electrodes shaped and spaced relative to one another to provide a spatial ion focusing and time-of-flight focusing of ions substantially independent of ion energy and on ion position in a plane transverse to said ion path.
11. The MR-TOF MS as defined in claim 1, wherein said ion mirror assembly includes one of a parallel assembly of conductive square frames, slotted plates, bars, and rods, each having an optional edge termination.

12. The MR-TOF MS as defined in claim 1, wherein at least a portion of said ion mirror assembly is operably connected to a pulsed voltage supply for gating ions in or out of the MR-TOF MS.
13. The MR-TOF MS as defined in claim 1, wherein said ion mirror assembly comprises at least two electrodes having voltages of opposite polarities relative to the other to form an attractive lens.
14. The MR-TOF MS as defined in claim 1, wherein said drift space comprises an ion deflector connected to one of a DC voltage supply and a pulsed voltage supply.
15. The MR-TOF MS as defined in claim 2, wherein said lens assembly includes at least two lenses elongated transversely to said ion path.
16. The MR-TOF MS as defined in claim 4, wherein said ion storage device comprises a gas-filled set of electrodes having a radio-frequency (RF) voltage applied to at least one of said electrodes.
17. The MR-TOF MS as defined in claim 4, wherein said ion storage device comprises a plurality of sets of electrodes having a radio frequency (RF) voltage applied to at least one electrode in a first set of electrodes and a pulse voltage applied to at least one electrode in a second set of electrodes.
18. The MR-TOF MS as defined in claim 4, wherein said ion accelerator comprises a pulsed orthogonal accelerator.
19. The MR-TOF MS as defined in claim 4, wherein said ion accelerator comprises a plurality of electrodes, each having a slit along said shift direction of the MR-TOF MS.

20. The MR-TOF MS as defined in claim 4, wherein said ion accelerator comprises one of a pulsed ion mirror assembly and a pulsed portion of said ion mirror assembly.
21. The MR-TOF MS as defined in claim 4, wherein said ion accelerator comprises one of an accelerator with pulsed voltages and an accelerator with static voltages.
22. The MR-TOF MS as defined in claim 5, wherein said continuous ion source comprises an intermediate ion storage guide preceding said ion storage device and having a gas pressure greater than said ion storage device.
23. The MR-TOF MS as defined in claim 5, wherein said continuous ion source comprises at least two gas-filled sets of electrodes having a radio-frequency (RF) voltage applied to at least one set of said gas-filled electrodes.
24. The MR-TOF MS as defined in claim 8, wherein said ion detector comprises one of a secondary electron multiplier having at least one dynode, a scintillator and photomultiplier, a micro-channel, micro-sphere plates, at least two channels of detection, and at least two anodes each connected to a data acquisition system having an analog-to-digital converter (ADC).
25. The MR-TOF MS as defined in claim 8, wherein said ion detector dynamic range is extended by alternating scans with various intensities of said pulsed ion source.
26. The MR-TOF MS as defined in claim 8, wherein said ion detector dynamic range is extended by alternating scans with varying durations of ion injection into an ion storage device.

27. The MR-TOF MS as defined in claim 9, wherein said gas-filled cell includes at least one electrode connected to a radio-frequency (RF) voltage for one of dampening ion kinetic energy in gas collisions, stabilizing internal ion energy, confining ions, fragmenting ions, selecting ion species and retaining ions for exposure to reactant particles.
28. The MR-TOF MS as defined in claim 14, wherein said ion deflector comprises at least one steering plate.
29. The MR-TOF MS as defined in claim 14, wherein said ion deflector is located on a far side of said shift axis opposite to said ion source for steering ions in a static mode to change direction of said ion path.
30. The MR-TOF MS as defined in claim 14, wherein said ion deflector is located on a similar side of said shift axis as said ion source for directing ions toward one of an off-axis detector and an MR-TOF MS analyzer, and revert in a direction of ion shift for a time of ion confinement within the MR-TOF MS.
31. The MR-TOF MS as defined in claim 16, wherein said gas-filled set of electrodes comprises at least one of an ion guide having a plurality of elongated rods, a 3-D quadrupole ion trap, a linear ion trap with ion ejection, an RF channel with at least one electrode having an opening for ion passage, a ring electrode trap, a hybrid ion guide with a 3-D ion trap, and a segmented analog of the aforementioned electrodes formed of at least two plates.
32. The MR-TOF MS as defined in claim 5, wherein said ion storage device includes one of a filter of ion components, a discriminator of ion components, and a suppressor of ion components.

33. A tandem time-of-flight mass spectrometer apparatus, comprising:
 - a pulsed ion source;
 - said MR-TOF MS of claim 1 provided to separate parent ions;
 - a fragmentation cell downstream of said MR-TOF MS for fragmenting the parent ions into daughter ions; and
 - a mass spectrometer downstream of said fragmentation cell for detecting said daughter ions;
 - wherein said at least one ion mirror assembly comprises two grid-less and parallel ion mirrors separated by a drift space and substantially elongated in one shift-direction.
34. The mass spectrometer apparatus as defined in claim 33, further comprising an ion selector subsequent said fragmentation cell.
35. The mass spectrometer apparatus as defined in claim 33, wherein said fragmentation cell comprises a gas-filled cell having a differential pumping stage and an ion focusing device.
36. The mass spectrometer apparatus as defined in claim 33, wherein said fragmentation cell comprises an internal gas pressure P associated with a cell length L ($P*L$) above 0.2 Torr*cm.
37. The mass spectrometer apparatus as defined in claim 33, wherein said fragmentation cell comprises a gas pressure $P > 0.5$ Torr and $L < 1$ cm.
38. The mass spectrometer apparatus as defined in claim 33, wherein said fragmentation cell comprises a gas filled set of electrodes having a radio frequency (RF) voltage applied to at least one of said electrodes for confining ions in radial direction.

39. The mass spectrometer apparatus as defined in claim 33, wherein said fragmentation cell further comprises a set of electrodes connected to one of a DC and slow-varying voltage to form an axial DC electric field, and an axial moving-wave electric field to control velocity of ion motion in said fragmentation cell, said DC voltage being applied to one of the same set of electrodes and a dissimilar set of electrodes.
40. The mass spectrometer apparatus as defined in claim 33, wherein said mass spectrometer downstream of said fragmentation cell comprises a time-of-flight mass spectrometer (TOF MS).
41. The mass spectrometer apparatus as defined in claim 40, wherein said TOF MS comprises an orthogonal ion accelerator.
42. The mass spectrometer apparatus as defined in claim 40, wherein said TOF MS comprises ion path less than, and an acceleration voltage greater than in said MR-TOF MS to produce an ion flight time in said TOF MS at least 100-fold less than in said MR-TOF MS.
43. The mass spectrometer apparatus as defined in claim 40, wherein said TOF MS comprises a data system adapted for parallel acquisition of daughter spectra without mixing spectra corresponding to different parent ions.
44. The mass spectrometer apparatus as defined in claim 40, wherein said TOF MS includes a first and a second multi-reflecting time-of-flight mass spectrometer (MR-TOF MS).
45. The mass spectrometer apparatus as defined in claim 44, wherein said second MR-TOF MS is substantially identical in construction to said first MR-TOF MS.

46. The mass spectrometer apparatus as defined in claim 41, wherein said orthogonal ion accelerator is grid-less.
47. The mass spectrometer apparatus as defined in claim 45, wherein the second MR-TOF MS forming said TOF MS comprises a plurality of deflectors cooperating with lenses in said drift space to adjust a flight path of the ions in said TOF MS.
48. A tandem multi-reflecting time-of-flight mass spectrometer (MR-TOF MS-MS) apparatus comprising:
- a first multi-reflecting time-of-flight mass spectrometer (MR-TOF MS) for separating parent ions;
 - a fragmentation cell attached to said first MR-TOF MS for receiving said parent ions; and
 - a second MR-TOF MS attached to said fragmentation cell for mass analysis of daughter ions exiting said fragmentation cell, wherein at least one of said MR-TOF MS comprises at least two grid-less and parallel ion mirrors separated by drift space and substantially elongated in one shift-direction,
- wherein at least one of said first and second MR-TOF MS comprises:
- an ion source;
 - an ion receiver downstream from said ion source;
 - at least one ion mirror assembly intermediate said ion source and said ion receiver and elongated in a shift direction for improving sensitivity and resolution of the MR-TOF MS;
 - a drift space intermediate said ion mirror assembly; and
 - a lens assembly disposed within said drift space along said at least one shift direction and with a period in said shift direction corresponding to ion shift per integer number of ion reflections,
 - said ion source, ion receiver, ion mirror assembly and said drift space arranged to provide a folded ion path between said ion source and

said ion receiver composed of at least one reflection by said ion mirror assembly for separating ions in time according to their mass-to-charge ratio (m/z) so that a flight time of the ions is substantially independent of ion energy.

49. (Canceled)

50. The tandem MR-TOF MS-MS apparatus as defined in claim 48, further comprising a timed ion selector between said first MR-TOF MS and said fragmentation cell.

51. The tandem MR-TOF MS-MS apparatus as defined in claim 48, wherein said fragmentation cell further comprises at least one set of electrodes connected to one of DC and slow varying voltage to form one of a respective axial DC electric field or an axial moving-wave electric field, controlling velocity of ion motion within said fragmentation cell, and said DC voltage being applied to at least one electrode in said at least one set as RF voltage.

52. The tandem MR-TOF MS-MS apparatus as defined in claim 48, wherein said fragmentation cell further includes a gas at a gas pressure (P) above $P \cdot L > 0.2 \text{ Torr} \cdot \text{cm}$.

53. The tandem MR-TOF MS-MS apparatus as defined in claim 48, wherein said fragmentation cell comprises a differential pumping stage and an ion focusing assembly.

54. The tandem MR-TOF MS-MS apparatus as defined in claim 48, wherein said fragmentation cell comprises at least one gas-filled set of electrodes having a radio frequency (RF) voltage applied to at least one electrode within said set of electrodes to confine ions in a radial direction.

55. The tandem MR-TOF MS-MS apparatus as defined in claim 48, wherein said fragmentation cell comprises means for ion storage and pulsed ejection, in one of an axial and an orthogonal direction.

56. The tandem MR-TOF MS-MS apparatus as defined in claim 52, wherein said second TOF MS comprises an orthogonal ion accelerator.

57. The tandem MR-TOF MS-MS apparatus as defined in claim 55, wherein said second MR-TOF MS comprises means for adjusting an ion path less than, and an acceleration voltage greater than, said first MR-TOF MS such that a flight time in said TOF MS is at least 100-fold less compared to said flight time in said first MR-TOF MS.

58. The tandem MR-TOF MS-MS apparatus as defined in claim 54, wherein said second MR-TOF MS comprises a data system providing parallel acquisition of daughter spectra without mixing spectra from unrelated parent ions.

59. The tandem MR-TOF MS-MS apparatus as defined in claim 58, wherein said second MR-TOF MS comprises a lens assembly disposed within said drift space.

60. The tandem MR-TOF MS-MS apparatus as defined in claim 59, wherein said lens assembly comprises at least one deflector configured to adjust a flight path of ions in said second MR-TOF MS.

61. A multi-reflecting time-of-flight mass spectrometer (MR-TOF MS-MS) apparatus comprising:

a multi-reflecting time-of-flight mass spectrometer (MR-TOF MS); and
a fragmentation cell connected said MR-TOF MS and configured to revert ions within said MR-TOF MS to employ the same MR-TOF analyzer for analysis of both

parent ions and fragment ions, wherein said MR-TOF MS comprises an assembly of two grid-less and parallel ion mirrors separated by drift space and substantially elongated in one shift-direction,

wherein said MR-TOF MS comprises:

- an ion source;
- an ion receiver downstream from said ion source;
- at least one ion mirror assembly intermediate said ion source and said ion receiver and elongated in a shift direction for improving sensitivity and resolution of the MR-TOF MS;
- a drift space intermediate said ion mirror assembly; and
- a lens assembly disposed within said drift space along said at least one shift direction and with a period in said shift direction corresponding to ion shift per integer number of ion reflections,

said ion source, ion receiver, ion mirror assembly and said drift space arranged to provide a folded ion-path between said ion source and said ion receiver composed of at least one reflection by said ion mirror assembly for separating ions in time according to their mass-to-charge ratio (m/z) so that a flight time of the ions is substantially independent of ion energy.

Election/Restrictions

The previous restriction requirement made by the examiner is withdrawn in view of the examiner's amendment authorized by applicant; all independent claims now substantially contain the limitations of claim 1, making restriction unnecessary.

Allowable Subject Matter

2. Claims 1, 3-48 and 50-61 allowed.
3. The following is an examiner's statement of reasons for allowance: As suggested by the examiner during the telephone interview, former dependent claims 2 and 10

would have been allowable if written in independent form including the base claim and any intervening claims. The applicant authorized an examiner's amendment to do this. Claim 2 contained the limitation "a lens assembly disposed within said drift space along said at least one shift direction and with a period in said shift direction corresponding to ion shift per integer number of ion reflections." The closest prior art to this limitation is Cotter, et al (U.S. Patent 5,202,563 A), which discloses a multi-reflecting time of flight mass spectrometer with an intermediate lens assembly (21 and 23 in Fig. 1); however this figure clearly shows two reflections with only one lens assembly, therefore the lens assembly does not have a period in the shift direction corresponding to the ion shift per integer number of ion reflections. The lens assembly in Cotter is also intended for a different purpose than the present invention, as the lenses in Cotter are deceleration 21 and acceleration 23 lenses to conduct ions into and out of a collision region 19. It therefore cannot be said that it would have been a matter of obvious design choice to provide additional lens assemblies to produce a period corresponding to ion shift per integer number of ion reflections. Claim 10 contains the limitation "wherein said ion mirror assembly comprises a plurality of electrodes shaped and spaced relative to one another to provide a spatial ion focusing and time-of-flight focusing of ions substantially independent of ion energy and on ion position in a plane transverse to said ion path." The closest prior art to this limitation is Kutscher, et al (U.S. Patent 5,017,780), which discloses an ion reflector that transversely focuses ions independent of ion energy (column 2, lines 35-40), but does not disclose doing so independent of ion position. Also, while Kutscher does anticipate combining multiple reflectors according to his

disclosure to provide a multi-reflecting time of flight mass spectrometer, the limitation that the assembly be "elongated in a shift direction" is clearly incompatible with the structure of the individual reflectors taught by Kutscher (see Fig. 1A). Nazarenko (SU 1725289) discloses such an elongated electrode structure, but, as explained in lines 19-27 on page 2 of applicant's specification, Nazarenko's structure does not focus across the plane of the ion path. A combination of Kutscher and Nazarenko is clearly unworkable, as the electrodes have entirely different shapes (Kutscher's electrodes are ring electrodes forming individual reflectors, while Nazarenko's electrodes are elongated bars forming a single extended reflector assembly).

4. Claims 1, 48 and 61 have been amended to include the limitations of claim 2, making them allowable as discussed above.
5. Claim 10 has been written in independent form, to include the limitations of claim 1 as it was written prior to the amendment, making it allowable as discussed above.
6. Claims 3-9 and 11-47 are allowable by virtue of their dependence from allowable claim 1.
7. Claims 50-60 are allowable by virtue of their dependence from allowable claim 48.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Maskell whose telephone number is 571/270-3210. The examiner can normally be reached on Monday-Friday 8AM-5PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Kim can be reached on 571/272-2293. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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09 January 2008



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